

Are preoperative hematologic parameters predictive of intraoperative bleeding in orthognathic surgery?

Hematologic parameters and intraoperative bleeding in orthognathic surgery

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Abstract

Aim: Orthognathic surgery is performed to correct dentofacial abnormalities and is generally known as a safe procedure with minimal bleeding. The purpose of this study was to evaluate whether the preoperative hematological parameters help predict intraoperative bleeding in orthognathic surgery.

Material and Methods: This retrospective study was performed with patients who underwent orthognathic surgery. Patients records were evaluated in terms of the demographics (gender, age, weight), duration of the surgery, amount of intraoperative bleeding, and the preoperatively routine complete blood count (CBC) parameters, especially PLT, MPV, MPV/PLT ratio, coagulation tests (PT, aPTT, INR) and NLR were recorded from patient files.

Results: The study included 101 patients with a mean age of 21.7 ± 4.8 years. The female to male ratio was 1.1 (52/49). The median duration of the operation was 270 minutes, ranging from 155 to 420 minutes. The amount of blood loss ranged from 90 to 820 ml in all subjects, with a median of 230 ml. The preoperative median hemoglobin value was 14.4 g/dL. PT, INR, aPTT, and weight were not independent predictors for the amount of bleeding. However, the duration of the surgery was an independent predictor for the amount of bleeding ($p < 0.001$). There was no correlation between the MPV/PLT ratio ($r = 0.003$, $p = 0.972$) and the neutrophil-to-lymphocyte ratio (NLR) ($r = -0.008$, $p = 0.935$) with the amount of bleeding (ml).

Discussion: Improving possible objective markers to predict intraoperative bleeding amounts is important for avoiding and managing the intraoperative bleeding complications for the surgery team in maxillofacial surgery. The results of this study demonstrated no correlation between preoperative hematologic normal ranged parameters such as PLT, MPV, MPV/PLT, NLR, PT, PTT, INR, and intraoperative bleeding in orthognathic surgery. Thus, caution in the preparation of patients and standardized preoperative procedures are essential to avoid undesirable intraoperative bleeding in orthognathic surgery.

Keywords

Intraoperative bleeding; Orthognathic surgery; MPV; Platelet

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Introduction

Orthognathic surgery is commonly preferred to correct dentofacial abnormalities for providing ideal functional, anatomic, and esthetic dental structures. Although a variety of procedures are being used by surgeons, Le Fort I Osteotomy and Sagittal Split Ramus Osteotomy (SSRO) are frequently applied together [1,2]. This group of surgical procedures is performed in anatomic areas that are rich in vessels. Thus intraoperative bleeding may occur during the surgery [3,4].

Orthognathic surgery is generally known as a safe procedure with a minimal amount of bleeding despite damaging major vessels. Although estimated blood loss has a wide range according to the type of surgery or varying reasons, it is generally accepted to be approximately 400 ml [4,5]. However, rarely severe bleeding can occur intraoperatively due to an injury to major vessels in the surgical field. Many reasons affect the bleeding including duration of operation, gender [6], weight [7], type of the anesthesia or surgery, surgeon [3,8]. Knowing the various interplays between these risk factors may provide an expectation of intraoperative blood loss, and this would improve preoperative patient management and ensure ideal planning and performance for surgery [9,10].

Several studies have described correlations between routine coagulation test results such as Activated Platelet Time (aPTT), Prothrombin Time (PT), with bleeding time. The relationship between routine coagulation tests and intraoperative bleeding has not been clearly shown. Routine coagulation screening is not suggested with no history of bleeding [2,9,10]. Recently, studies have focused on thrombo-elastography (TEG), which is a predictor of intraoperatively blood loss. TEG methods are used to analyze the viscoelastic properties of whole blood samples and the interaction among coagulation factors and inhibitors such as fibrin clot properties, blood cells, and fibrinolytic factors. But it is an expensive procedure for hospitals [2,10]. Therefore, improving an inexpensive method or tool for predicting intraoperative bleeding may be useful. Today, several new size-related parameters have been introduced to the routine complete blood count (CBC). Automated blood cell counters are able to provide a platelet (PLT) count and derived indices relating to Mean Platelet Volume (MPV). PLT's effect on clotting is scientifically known information. Furthermore, the MPV is accepted as an indicator of platelet activation and has recently become more important than PLT [11]. High MPV values represent larger and reactive platelets. In the literature, researchers reported that MPV could provide information about preoperative assessment for potential bleeding [12].

The investigators hypothesized that evaluating preoperative PLT, MPV, MPV/PLT, PT, aPTT, INR, and NLR maybe informative regarding intraoperative bleeding risk, and thus provide a prognosis to the surgery team, helping to facilitate intraoperative patient management. The purpose of the study was to determine whether the preoperative PLT, MPV, MPV/PLT ratio, PT, aPTT, INR and NLR are predictors for intraoperative bleeding.

Material and Methods

Study Design and Samples

The investigators designed and implemented observational and

retrospective clinical research. The study protocol followed the Declaration of Helsinki on medical research protocols, and the Ethics Committee approved the study. The study was performed between January 2014 and August 2016, who had undergone orthognathic surgery. To be included in the study sample, ASA I-II (American Society of Anesthesiology Classification) patients who were performed orthognathic surgery due to maxillary and/or mandibular malformations such as deficiency, excess, or asymmetries, to improve occlusion, facial balance, and airways, were listed as the inclusion criteria. Patients who had a hematological disease associated with excess bleeding, or using any antiaggregants, antiplatelets and bleeding-reducing agents were excluded from the study.

Intervention and study variables

Patient data from a total of 101 patients were collected from the file records. The patient demographics such as gender, age, weight, duration of the surgery, and amount of bleeding were recorded. The routine CBC included White blood cell (WBC), hemoglobin (HGB), red blood cell (RBC) count, N (neutrophil), lymphocyte (L), hematocrit (HCT) levels, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), RBC (red blood cell count), red blood cell distribution width (RDW), MPV, PLT were recorded. Also, aPTT, PT, and INR that showed the coagulation status of the patient were recorded from files.

Anesthetic Protocol

A standardized general anesthesia method was preferred for all patients. Preoperative evaluation was made by the same anesthesiologist. Routine blood analysis was studied before the surgery. All patients were premedicated with intravenous midazolam just before the operation. A standard hypotensive anesthetic method was applied for less bleeding. For the anesthetic induction, 1 mcg/kg fentanyl and 2-3 mg/kg propofol were applied intravenously. To facilitate the nasotracheal intubation, 0.6 mg/kg of rocuronium was applied and repeated if immobility during the operation was needed. Anesthesia was maintained under intermittent positive-pressure ventilation, using a mixture of air and oxygen (50%:50%), and sevoflurane. Providing hypotensive anesthesia, esmolol infusion was applied to maintain an optimal systolic blood pressure of 80 to 100 mm Hg (approximately 20% below normal) during the surgery. Standard noninvasive monitoring procedures were applied with oxygen saturation, non-invasive blood pressure, electrocardiogram, and end-Tidal CO₂ (CO₂ level after tidal volume). Intraoperative fluid management consisted of intravenous administration of 0.09% NaCl (saline) during the procedure. Neostigmine (0.08 mg/kg) and atropine (0.01 mg/kg) were used intravenously at the end of the operation to reverse the neuromuscular block, and then the patient was extubated. After the operation, during recovery, the patients were followed up by the post-anesthesia care unit (PACU) and were admitted to the inpatient service.

Surgical Procedure

Buccal infiltrative anesthesia of the maxillary anterior walls and pterygoid plates in the maxilla and bilateral mandibular blocks along with infiltrative anesthesia of the posterior sulcus in the mandible was applied to all patients using 1/1 diluted eight ampoules with 2% articaine and with 1:100.000 epinephrine solution (80 mg) (Ultracain® 2% Ampoule, Sanofi Aventis,

Istanbul, Turkey) 10 minutes before both Le Fort I and sagittal split ramus osteotomies (SSRO) in all patients.

A horizontal incision was made between the second premolars in the vestibular sulcus of the maxilla. Maxillary anterior and lateral walls and pterygoid plates were exposed to the lower level of infraorbital foramen. The horizontal osteotomy was made using a Piezosurgery (Mectron, Italy) at the level of the nasal floor at a safe distance (~5 mm) from the apices of the teeth. Pterygoid plates were separated using a curved pterygoid osteotome. Lateral nasal walls and nasal septum were also separated with osteotomies. Down-fracture of the maxilla was performed with the help of a bone hook at the anterior, and a bone spreader at the posterior aspect of the maxilla. Tessier mobilizers were then used to pull the maxilla forward. Remaining bony bridges at the posterior aspect of the maxilla were transected under direct vision and soft tissues were protected to minimize bleeding. Maxillo-mandibular fixation was performed to position the maxilla to the desired relationship with the mandible using a surgical splint. Four L-shaped mini plates were placed along with the pyriform aperture and the zygomaticomaxillary buttress.

A full-thickness incision was made just lingual to the external oblique ridge, halfway up the mandibular ramus superiorly to the mesial of the second molar inferiorly. Subperiosteal dissection was carried to allow adequate visualization of the body and mandibular ramus. Medial ramus, sagittal and buccal osteotomies were made using a Lindeman bur. Chisel osteotomies were used to deepen the osteotomy cut through the cortical bone. A lower border separator at the lower end of the buccal osteotomy and a bone spreader at the sagittal osteotomy were used to split the distal and proximal bone segments of the mandible. Care was taken not to injure the inferior alveolar nerve during the split. Maxillo-mandibular fixation was performed to position the mandible to the final relationship with the maxilla using the second surgical splint. Mini plates were placed to fixate the distal and proximal segments.

The amount of bleeding was calculated using the volume of suctioned fluids and total irrigation solution and weighing the gauze during the operation, and noted.

Data Analyses

Descriptive statistics were presented as mean \pm standard deviation or median (min-max) depending on the normal distribution of the variables. Categorical variables were expressed as numbers and percentages. The Kolmogorov-Smirnov test and the Shapiro-Wilk test were used to check the normality of the numerical variables. In a comparison of the two independent groups, the Mann-Whitney U test was used when the numerical variables did not distribute normally. We evaluated possible correlations between the amount of bleeding and hematologic parameters using the Spearman correlation coefficient. Univariate and multivariate linear regression models were used to evaluate the factors that affected the amount of surgery related to bleeding. Receiver operating characteristics curve (ROC) analysis was used to evaluate the predictive ability of a certain platelet count cut-off to predict the increased amount of surgery-related bleeding. The Youden index, optimal cut-off point, 95% confidence interval, and area under the curve

(AUC) were calculated by the DeLong method with the Medcalc Statistical Software trial version. "Jamovi project (2020), Jamovi (Version 1.2.22) [Computer Software] (Retrieved from <https://www.jamovi.org>) and JASP (Version 0.13) (Retrieved from <https://jasp-stats.org>) were used for statistical analyses. A p-value <0.05 was accepted as statistically significant.

Results

A total of 101 patients with a mean age of 21.7 ± 4.8 years were included in the study. The female to male ratio was 1.1 (52/49) of patients. Demographics, clinical and laboratory characteristics of the study group are given in Table 1. The median duration of the operation was 270 minutes, ranging from 155 to 420 minutes. The amount of bleeding ranged from 90 to 820 ml in all subjects, with a median of 230 ml. However, the need for perioperative blood transfusion was not detected in any patient. There was a positive correlation between the duration of the operation and the amount of bleeding ($p < 0.001$). The preoperative median hemoglobin value was 14.4 g/dL. Although the median white blood cell count was 7.3×10^3 cell/ μ L, it ranged from 3.9 to 24.3×10^3 cell/ μ L. The platelet count (PLT) with its minimum and maximum values was within the normal reference values. In the study group, the median NLR and MPV were calculated as 2.2 with a range of 1.1 to 15.5 and 0.03 with a range of 0.02 to 0.07. The median values of PT and INR were within the normal range. The linear regression analysis determined the independent predictors of the amount of intraoperative bleeding (Table 2). None of the included parameters in Table 2 were independent predictors of intraoperative bleeding.

None of the studied hematologic parameters showed a significant correlation with the amount of intraoperative bleeding (Table 3).

Table 1. Demographics and clinical and laboratory characteristics of the study group

Age (years)	21.7 \pm 4.8
Sex	
Male	49 (48.5)
Female	52 (51.5)
Body weight (kg)	66.8 \pm 15.7
Duration of surgery (minutes)	270 [155 – 420]
Amount of bleeding (mL)	230 [90 – 820]
Preoperative hemoglobin (g/dL)	14.4 [9.4 – 17.3]
White blood cell count ($\times 10^3$ cell/ μ L)	7.3 [3.9 – 24.3]
Platelet count ($\times 10^3$ cell/ μ L)	268 [142 – 454]
Neutrophil count ($\times 10^3$ cell/ μ L)	62.6 [44 – 89.8]
Lymphocyte count ($\times 10^3$ cell/ μ L)	28.2 [5.7 – 42.3]
Neutrophil-to-lymphocyte ratio (NLR)	2.2 [1.1 – 15.5]
RBC count ($\times 10^6$ cell/ μ L)	5 [3 – 6]
Hematocrit (%)	43.7 [26.6 – 53.8]
MCV (fL)	87.4 [64.3 – 96.3]
MPV	7.8 [6 – 12]
MPV/Platelet ratio	0.03 [0.02 – 0.07]
RDW (%)	13.4 [9.7 – 18.3]
Prothrombin time (seconds)	11.3 [9.9 – 15.6]
INR	1.1 [0.9 – 1.7]
aPTT (seconds)	27.3 [19.2 – 33.8]

Descriptive statistics were presented as median [min-max], mean and standard deviation and number (%).

In addition, neither NLR, nor MPV/platelet ratios were significantly correlated with coagulation parameters including PT, INR, and aPTT. Furthermore, a schematic representation of density and correlation between the amount of bleeding (ml) and MPV/platelet ratio ($r=0.003$, $p=0.972$) and neutrophil-to-lymphocyte ratio (NLR) ($r=-0.008$, $p=0.935$) are given in Figure 1 and Figure 2, respectively.

Table 2. Linear regression analysis showing independent predictors of operation related bleeding

	Crude Beta [95%CI]	Crude p-value	Adj. Beta [95%CI]	Adj. p-value
Body weight	1.92 [0.34 – 3.49]	0.019	1.46 (-0.06 – 2.98)	0.063
Duration of surgery	0.81 [0.38 – 1.24]	< 0.001	0.69 (0.25 – 1.13)	0.003
Platelet count	-0.42 (-0.82 – -0.02)	0.044	-0.23 (-0.62 – 0.16)	0.253
aPTT	0.2 [-12.23 – 12.63]	0.975	-	-
Prothrombin time	10.87 [-16.86 – 38.6]	0.444	-	-

Adj.: Adjusted, aPTT: activated partial thromboplastin time

Table 3. Correlations between the amount of surgery related bleeding and hematologic parameters

	Amount of bleeding (mL)	
	r	P-value
MPV/Platelet ratio	0.003	0.972
Neutrophil-to-lymphocyte ratio	-0.008	0.935
Preoperative hemoglobin (g/dL)	0.177	0.077
White blood cell count (x103cell/ μ L)	-0.099	0.324
Platelet count (x103cell/ μ L)	-0.083	0.408
Neutrophil count (x103cell/ μ L)	-0.042	0.676
Lymphocyte count (x103cell/ μ L)	-0.031	0.757
RBC count (x106cell/ μ L)	0.176	0.079
Hematocrit (%)	0.150	0.135
MCV (fL)	-0.062	0.540
MPV	-0.193	0.053
RDW (%)	0.184	0.066
Prothrombin time (seconds)	0.008	0.935
INR	0.020	0.845
aPTT (seconds)	-0.005	0.957
Spearman's rho		

Discussion

Orthognathic surgery aims to correct dentofacial malformations, is a complex procedure with potential blood loss and complications. Although it is generally a safe surgery in terms of bleeding, not only do some authors find major blood loss to be particularly associated with double-jaw surgery with interpositional bone grafting, but others also associate it with the complexity and prolonged duration of procedures [15-17]. Well-known knowledge of the basic anatomy of bimaxillary surgery, the development of instrumentation specifically designed for the operation, and the use of hypotensive anesthesia techniques have significantly decreased blood loss, morbidity, and transfusion requirements [15,18,19]. The consensus found in the literature reviewed was that orthognathic surgery should be performed under general hypotensive anesthesia [15,17-19]. Hypotensive anesthesia

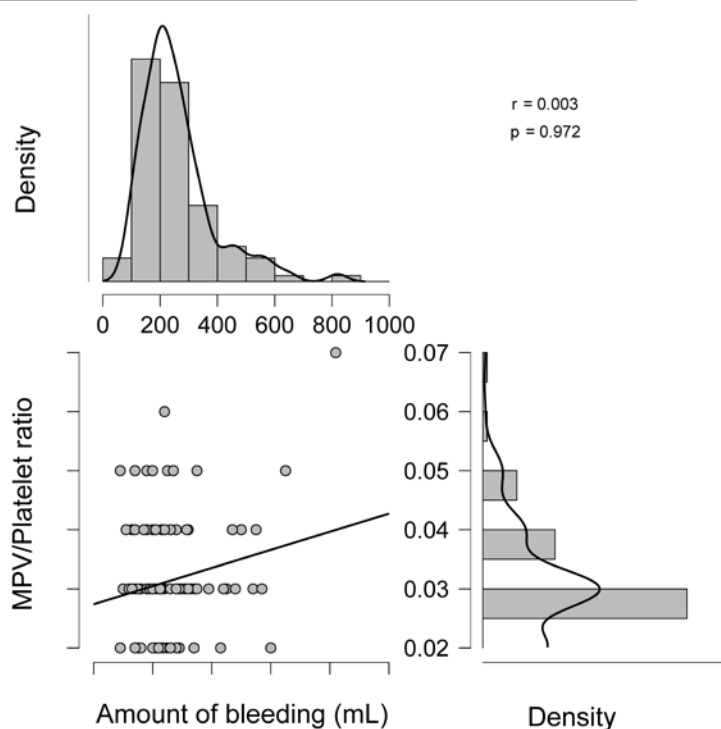


Figure 1. Schematic representation of density and correlation between the amount of bleeding (ml) and MPV/platelet ratio ($r=0.003$, $p=0.972$).

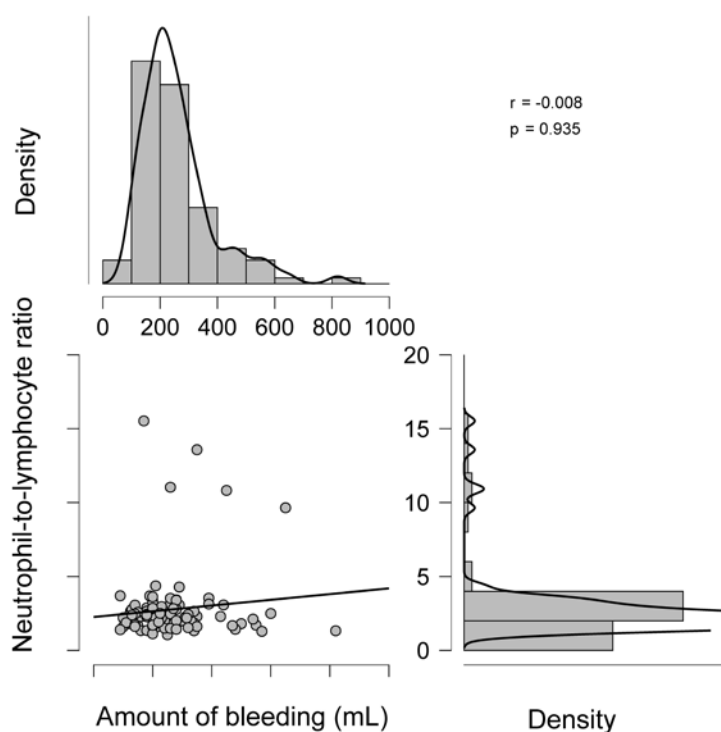


Figure 2. Schematic representation of density and correlation between the amount of bleeding (ml) and neutrophil-to-lymphocyte ratio ($r=-0.008$, $p=0.935$).

was shown to improve the visual quality of the surgical field in orthognathic surgery. Despite hypotensive anesthesia, blood loss increased gradually with prolonged operation time [19]. In this study, it has been determined that the duration of the surgery affected the amount of bleeding with a positive correlation, but preoperative hematological parameters in the normal range were not related to bleeding in the intraoperative period. Prediction of intraoperatively bleeding before the

procedure in orthognathic surgery is important for maxillofacial surgeons to provide better patient management. Similar to the literature, esmolol infusion was administered to all patients to reduce or control the surgery-related bleeding as a standard hypotensive anesthesia method. Moderate hypotension was provided during the surgery and the amount of median bleeding ranged was found to be 230 ml, which is reported as 400 ml in the literature [4,5]. No need for intraoperative or postoperative blood transfusion was required in such a young patient population in terms of avoiding the transmission of disease or graft versus host reactions.

The experience of the surgeon is a factor to determine the total bleeding amount during the surgical procedures, which includes compressing the area with gauze and ligating the vessels [5]. A good knowledge of anatomy and surgery experience of the surgeon may prevent major bleeding during surgery [20]. In this retrospective study, the surgery was performed at the same surgery times, thus differences between the personal applications have been eliminated.

The normal clotting mechanism includes vascular mechanisms, platelets, coagulation factors, some prostaglandins, enzymes, and proteins. Primary hemostasis is the formation of a weak platelet plug is achieved in four phases: vasoconstriction, platelet adhesion, platelet activation, and platelet aggregation. Secondary hemostasis is actualized, which involves the coagulation cascade. First, the activation of clotting factors is triggered, and then conversion of prothrombin to thrombin and conversion of fibrinogen to fibrin occurs. At the end of the clotting mechanism, fibrin, the functioning form of fibrinogen, stabilizes this weak platelet plug [21]. PLT count is the main factor for intraoperatively bleeding. MPV symbolizes the volume of the platelets, and is an indicator of platelet activation [11]. The MPV measurement may reflect either the level of platelet stimulation and platelet production rate. Larger platelets are more adhesive and provide better aggregation than smaller ones [11,22]. Furthermore, laboratory-testing involving aPTT or PT/INR reflect the bleeding time, and does not affect primary hemostasis. PTT shows the intrinsic pathway of secondary hemostasis, and the PT/INR shows the extrinsic pathway of secondary hemostasis [22]. The purpose of the study was to research the relationship between the preoperative hematological parameters especially PLT, MPV, MPV/PLT, PT, PTT, and INR with bleeding. The relationship was found to be meaningless in normal ranged preoperative values. The importance of this study was that mentioning preoperative evaluation and providing a certain standardization may ensure a successful orthognathic surgery procedure with less bleeding. In summary, preoperative patient preparation with anamnesis, examination, and laboratory tests is essential to avoid surgery or anesthesia-related complication in surgery clinics.

Praveen et al. [15] compared hypotensive and normotensive anesthesia procedures to determine the differences in terms of bleeding and reported the average bleeding as 200 mL (maximum 400 ml) in the hypotensive group and 350 mL (maximum 1,575 mL) in the normotensive group, whereas in our study, it was 230 ml. Some researchers preferred to use some medications that reduce bleeding, such as tranexamic acid [23]. No patients were administered bleeding-reducing medications

in this study.

Point-of-care testing of hemostatic function such as thromboelastography, thromboelastometry, and platelet function assays allow specific targeted therapy of coagulopathy [24]. Not using this methods may be a limitation of this study.

Conclusion

Improving possible objective markers to predict intraoperative bleeding amounts is important in avoiding and managing the intraoperative bleeding complication for the surgery team in maxillofacial surgery. This present study demonstrated no correlation between preoperative hematologic parameters in normal ranges such as PLT, MPV, MPV/PLT, NLR, PT, PTT, INR, and intraoperative bleeding in orthognathic surgery. Therefore, caution to evaluate patients preoperatively and providing good standardization is essential to avoid undesirable bleeding in orthognathic surgery. Further prospective studies on this topic should include larger populations.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest

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